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# Forecasting of the Possible Outcome of Prosthetics of the Aortal Valve on Preoperational Anatomic-Functional Hemodynamics and According to Heart Indicators

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## 1. Introduction

Prosthetics of the aortal valve is recommended as a standard surgical procedure for the majority of patients with defects of the aortal valve, who need surgical treatment [1]. Being the most simple technically possible to make nowadays, prosthetics of the aortal valve makes 13 % from all operations in case of acquired valve defects [2,3]. The 5-year survival rate without operation makes 50-80 % whereas surgical treatment leads to recovery and survival rate increase even at a serious clinical course of aortal defect [4,5,6]. At present stage of cardiosurgery development there are some methods of estimation of risk of operation [7,8,9]. However indicators under which it would be possible to estimate the forecast of AV prosthetics in the postoperative period are quite poor [10,11]. Available scales of risk estimation sometimes limit an exact prediction of risk or overrate the risk at patients who undergo valve surgery with or without coronary shunting [12,13,14,15]. The estimation of preoperative indicators which characterize the postoperative forecast can be useful for preoperative stratification of risk.

The aim of the research was to estimate the influence of initial anatomic-functional and hemodynamic indicators when forecasting the nearest results at patients after prosthetics of the aortal valve.

## 2. Material and methods

To estimate the influence of initial anatomic-functional indicators on the results of AV prosthetics 394 patients who underwent isolated AV prosthetics in 2001-2007 have been examined. Out of 394 people there are 311 men and 83 women at the age of 10 - 78, middle age is  $36,9 \pm 1,3$  years. In Functional Class I on New York Heart Association there were 14 (3,6 %) patients, in class II - 42 (10,7 %), in class III - 296 (75,0 %), in class IV - 42 (10,7%). Patients have been divided according to hemodynamic implication of defect into two

groups: I group patients with an aortal stenosis and combined aortal defect with prevalence of stenosis (AS) - 165 (41,9 %) patients and II group with aortal insufficiency and combined aortal defect with prevalence of insufficiency (AI) - 229 (58,1 %) patients. The reasons of aortal defect (AD) were: rheumatic disease in 74,8 % of cases, an infectious endocarditis (IE) - 16,3 %, congenital defect AV - 8,5 %, an atherosclerotic degeneration and a calcification - 0,4 %. All patients took chest X-ray, ECG, EchoCG, laboratory examination. Patients condition at baseline was a landmark to determine all totality of defect pathogenetic disorders, and evaluation of the factors affecting the separate components of complete clinical picture creation permitted to consider specially the causes, conditions and consequences of systemic positions.

Calculations were performed with the help of «STATISTICA for Windows», v.6.0 and original programs developed in "Excel - 2000" in "Visual Basic for Application" integrated computer language. Group data was divided into numeral and classification ones; additional tables for deviations (abs. and %) of variables from baseline levels were calculated. Difference of significance was evaluated by  $\chi^2$ -criterion and 2x2 tables - by adjusted Fisher test.

Distribution parameters were evaluated by formulas as follows:

$$M = \frac{1}{N} \sum_{i=1}^n X_i; \quad S = \sqrt{\frac{1}{N-1} \sum_{i=1}^n (X_i - M)^2}; \quad m = M \frac{S}{\sqrt{N}}$$

Consistency of numerical data with normal distribution law was assessed with help of Kolmogorov test. If the numerical data did not correspond to normal distribution law, non-parametric statistical methods were used - Wilcoxon rank test. Power and direction of correlation between the signs were determined by Pearson correlation coefficient (**r**) and by Spearmanrank correlation, if distribution of the baseline data was deviant. The values of these tests range from -1 to +1. The extreme values are observed in signs associated with linear functional relation. The significance of selected correlation coefficient is assessed by statistics value:  $r^* \sqrt{n-2} / \sqrt{1-r^2} = t_{a,f(1)}$ . The expression (1) permits to determine *a*, possibility of correlation coefficient difference from zero depending on *r* and sample size *n*. This, in turn, allows comparing the correlation of the same signs in the different sample sizes by possibility. Correlation power was assessed by a value of the correlation coefficient: strong, if  $r \geq 0.7$ , moderate, if  $r = 0.3-0.7$ , weak, if  $r < 0.3$ . The differences between compared values were significant if  $p < 0.5$ , it is consistent with criteria accepted in medical and biological researches.

Prognosis model is based on the regression analysis. Regression analysis was directed to the test of significance of one (dependent) variable *Y* from set of other ones, so called independent variables  $X_j = \{X_1, X_2, \dots, X_p\}$ . The values of the prognostic parameter are defined according to the result of determination of the risk factors based on analysis of the clinical materials. The purpose of linear regression analysis in this study was to predict the values of the resulted variable *Y* according to the known values of physical parameters, EchoCG parameters and various additional features related to surgery specificity. The index of favorable surgery outcome was calculated as an arithmetic mean of risk factors.

As a result of these calculations, the model was developed. Based on this model the program was created in "Excel-2000" - « The Program of forecasting of probability of a favorable outcome of surgical treatment of aortal valve defects » (CERTIFICATE SPD RUzbDGU 01377) which helps to calculate a percentage of favorable surgery outcome and dynamics of LV ejection fraction after surgery with prognostic significance of 75-90%.

### 3. Results

As a result of the performed analysis the variables put into factor groups (F) affecting the surgery prognosis were determined: F1 - blood supply disturbance (HF, NYHA FC), F2 - physical parameters (gender, age\*, weight\*, height\*, body surface area\*, Kettle index\*, CTI\*), F3 - hemodynamic parameters (SBP\*, DBP\*, MBP\*, BSV, HR\*, BMV\*, TPR\*, SPR, HI\*, LV stroke work\*), F4 - heart parameters (EDD\*, ESD\*, EDV\*, ESV\*, SV\*, EF\*, FS\*, RF\*, SVE\*, RV\*, LA\*, RA\*, PA\*), F5 - myocardial parameters (IVS\*, LVPW\*, LVMM\*, sPLVWT and dPLVWT\*, 2HD\*), F6 - valve morphology (calcification degree on AV, regurgitation degree on AV, MV, and TV), F7- - valve parameters (FA and ascending aorta diameter\*, AV gradients\*, AO\* surface, MO\* surface, MV gradients\*, Emv, Amv, E/A mv). Indexed parameters, reverse values and second degree were considered in «\*» variables, it has been leading to increase in prognosis efficacy (see Table 1).

During research it has been defined, that for patients with isolated AV prosthetics greater influence on the operation forecast was made by factors heart characteristics, the central hemodynamics, indicators of valves, anthropometrical data and myocardium indicators (Fig. 1)

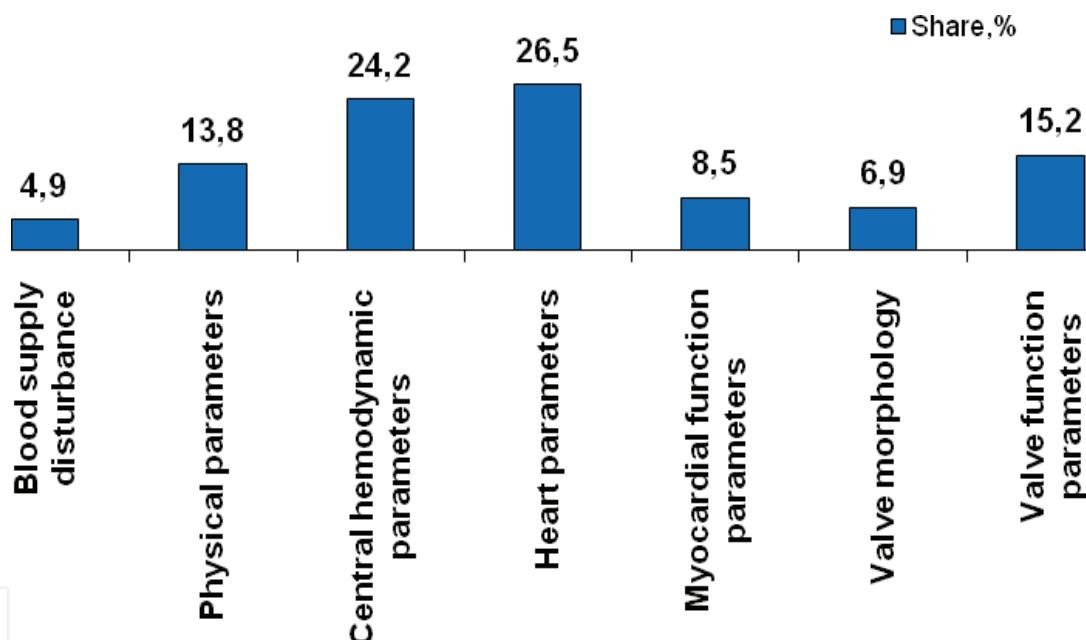


Fig. 1. Share of influence of factors on the forecast

N <sub>o</sub>	Variable	Unit	defenition	Variable nomenclature
<b>I Blood supply disturbance (F 1)</b>				
1	HF		I, IIA, IIB, III	Heart failure
2	FC		I, II, III, IV	Functional class
<b>II Physical parameters (F 2)</b>				
1	Gender		1 - man, 2 - woman	Patient gender
2	Age*	years		Age
3	Weighr*	kg		Weight
4	Height*	cm		Height

No	Variable	Unit	defenition	Variable nomenclature
5	BSA*	m <sup>2</sup>	$BSA = 0.007184 * \text{Weight}^{0.423} * \text{Height}^{0.725}$	Body surface area
6	Ketle index*	U	$\text{Ketle index} = 10000 * \text{Weight} / \text{Height}^2$	Ketle index (body weight index)
7	CTI*	%		Cardiothoracic index
<b>III Central hemodynamic parameters (F 3)</b>				
1	SBP*	mmHg		Systolic blood pressure
2	DBP*	mmHg		Diastolic blood pressure
3	MBP*	mmHg	$MBP = DBP + [(SBP - DBP) / 3]$	Mean blood pressure
4	PBP*	mmHg	$SBP - DBP$	Pulse blood pressure
5	BSV		$BSV = 90,97 + 0,54 * PBP - 0,57 * DBP - 0,61 * \text{Age}$	Blood stroke volume by Starr (39)
6	HR*	beat per minute		Heart rate
7	CO*	l/min	$CO = SV * HR / 1000$	Cardiac output (blood supply)
8	TPR*	dyne*cm <sup>-5</sup>	$TPR = 79,92 * MBP / CO$	Total peripheral resistance (59)
9	RPR		$RPR = TPR / BSA$	Relative peripheral resistance (110)
10	HI*	U	$HI = CO / BSA$	Heart index (109)
11	Asw*	U	$Asw(LV) = SV * 1,055 * (MBP - 5) * 0,0136$	LV stroke work (153)
12	LVMW	U	$LVMW = 0,0136 * 1,055 * CO * (MBP - 5)$	LV minute work (157)
13	LVWI		$LVWI = 0,0136 * 1,055 * HI * (MBP - 5)$	LV work index (160)
14	LVWSI		$LVWSI = 0,0136 * 1,055 * SI * (MBP - 5)$	LV work stroke index (161)
15	HF <sub>i</sub>		$HF_i = SBP * HR / LVMM$	Heart functioning index
<b>IV Heart parameters (F4)</b>				
1	EDD*	cm		End-diastolic dimension
2	ESD*	cm		End-systolic dimension
3	EDV*	cm <sup>3</sup>	$EDV = 7 * EDD^3 / (2.4 + EDD)$	End-diastolic volume
4	ESV*	cm <sup>3</sup>	$ESV = 7 * ESD^3 / (2.4 + ESD)$	End-systolic volume
5	SV*	cm <sup>3</sup>	$SV = EDV - ESV$	Stroke volume
6	SI*	u	$SI = SV / BSA$	Stroke index (108)
7	LVEF*	%	$LVEF = 100 * (EDV - ESV) / EDV$	Ejection fraction
8	LVFS*	%	$LVFS = 100 * (EDD - ESD) / EDD$	Fractional shortening
9	RF	%	$RF = ESV / EDV * 100$	Residual fraction (55)
10	SVE*	%	$SVE = EDV / ESV * 100$	Systolic ventricular ejection (56)

No	Variable	Unit	defenition	Variable nomenclature
11	TC*		$TC = (EDV-ESV) / ((EDD-ESD)*1/ESV)$	Ventricular wall tensility coefficient (57)
12	RV*	cm		Right ventricle
13	LA*	cm		Left atrium
14	RA*	cm		Right atrium
15	PA*	cm		Pulmonary artery
16	PAP	mmHg		Pulmonary artery pressure
17	PA FAD	mm		PA fibrous annulus diameter
<b>V Myocardial function parameters (F5)</b>				
1	dIVST*	cm		Diastolic interventricular septum thickness
2	dPLVWT*	cm		Diastolic posterior LV wall thickness
3	LVMM*	g	$LVMM = 1,04 * ((EDD+VST+PLVWT)^3 - EDD^3) - 13,6$	LV myocardial mass
4	rsPLVWT*	U.	$rsPLVWT = dPLVWT / EDD$	Relative systolic posterior LV wall thickness
5	rdPLVWT*	U.	$rdPLVWT = dPLVWT / ESD$	Relative diastolic posterior LV wall thickness
6	2HD*	U.	$2HD = (dIVST + dPLVWT) / EDD$	Relative double thickness
<b>VI Valve morphology (F 6)</b>				
1	AVca	score	1,2,3,4	AV calcification, degree
2	AVreg	score	1,2,3,4	AV regurgitation, degree
3	MVreg	score	1,2,3,4	MV regurgitation, degree
4	TVreg	score	1,2,3,4	TV regurgitation, degree
<b>VII Valve function parameters (F 7)</b>				
1	ARD*	cm		Aortic root diameter
2	AAD*	cm		Ascending aorta diameter
3	AVppg*	mmHg		AV peak pressure gradient
4	AVmpg*	mmHg		AV mean pressure gradient
5	AVsfs	m/s		AV systolic flow speed
6	AO s*	cm <sup>2</sup>		Aortic orifice surface area
7	E mv			MV E peak
8	A mv			MV A peak
9	E/A mv	U.	$E/A mv = E mv / A mv$	E/A ratio
10	MO s*	cm <sup>2</sup>		Mitral orifice surface area
11	MV ppg	mmHg		MV peak pressure gradient
12	MV mpg	mmHg		MV mean pressure gradient

Table 1. Risk factors and variables and their components



During the correlation analysis of relation of factors with the operation forecast the following patterns have been revealed.

The moderate force of correlation of blood supply disturbance indicators (**F1**) ( $r=0,683$ ) with the operation forecast has been revealed. It is accounted for the fact that among the operated patients there were more patients at a serious stage of HF and FC, age-specific patients with the long rheumatic anamnesis complicated with a current aortal defect and acute IE. Thus the bigger dependence of the operation forecast on circulatory unefficiency indicators was in the group of patients with AI ( $r=0,707$ ), than in the group of patients with AS ( $r=0,580$ ). The less was HF ( $r = -0,346$ ) and FC degree on NYHA ( $r = -0,606$ ), the more favorable there was an operation forecast (Fig. 2).

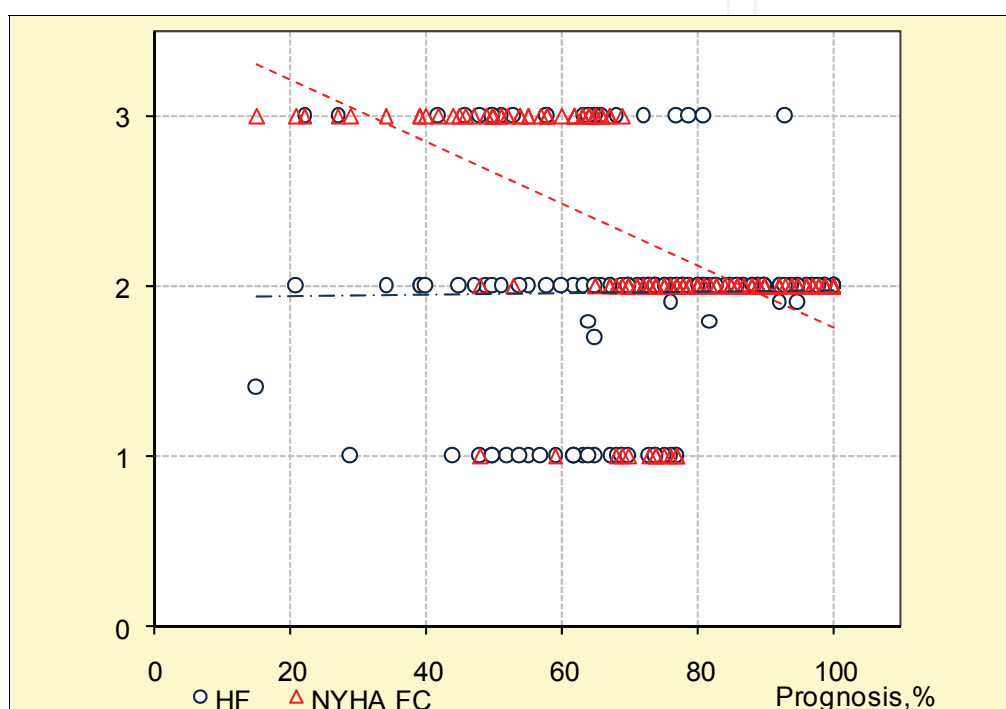


Fig. 2. Influence of degree HF and FC NYHA on the operation forecast

The analysis of the influence of physical parameters indicators (**F2**) has shown, that the younger the patient was ( $r = -0,626$ ) and the less Kettle index ( $r = -0,324$ ) and CTI ( $r = -0,584$ ) were, at appropriate height ( $r=0,385$ ) (that testifies the constitutional maturity of the patient), the more accurate the operation forecast was. Whereas the indicator of body surface had very weak correlation ( $r = -0,011$ ), that is bound up with the absence of patients with «prosthesis-patient mismatch» in the surveyed group. In hemodynamic groups the correlation was discernible. Dependence of the operation forecast on CTI was shown at patients with AI ( $r = -0,567$ ) more than at patients with AS ( $r = -0,298$ ). The great values of indicator CTI shown by radiological signs of a LV arch protrusion on the left side contour and an aortic arch on the right side contour of a heart shade arise and testify the evidence of aortal defect that is observed at patients who suffer from AV insufficiency. In both groups the patients of the young-age group had more accurate operation forecast. However the influence of an indicator of the body surface area with the forecast was observed more at patients with AS ( $r=0,363$ ), than at patients with AI ( $r = -0,184$ ). If to estimate influence of age on peak AV mpj in both groups then the value was higher in the senior age group (AI  $r = 0,470$ ;

AS  $r = 0,612$ ). The loss of aorta elasticity at the expense of sclerotic processes, which occur after a number of years, leads to increase of AV mpg value.

The analysis of influence of hemodynamic parameters indicators (**F3**) has shown, that hemodynamic indicators had moderate correlation with the operation forecast ( $r=0,424$ ). The patients with the big stroke output of blood circulation had the best operation forecast, which means indemnification and adequate regulation of the central hemodynamic. Thus the influence of indicators (F3) on the operation forecast was more in group of patients with AI ( $r=0,232$ ), than in a subgroup with AS ( $r=0,124$ ).

The analysis of influence of heart parameters (**F4**) on the operation forecast has shown that the linear and LV volume indicators have direct correlation with SV and LV EF indicators. The patients with LV sufficient volume indicators at smaller changes on a small circle of blood circulation had more accurate operation forecast (Fig. 3).

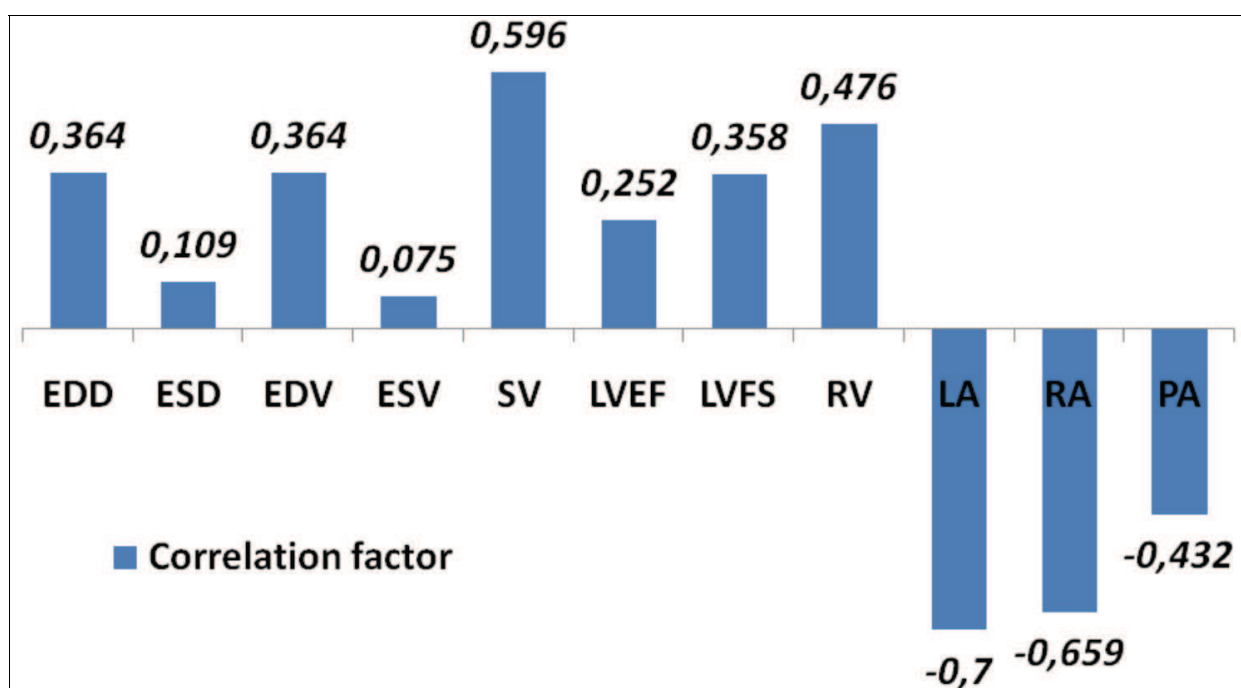


Fig. 3. Correlation of an indicator with an operation outcome

One of the important indicators was the indicator of SV size. The more the SV size was, the more accurate an operation forecast in groups was.  $SV = (EDV_{LV} - ESV_{LV})$  size mostly depends on ESV size, which characterizes the force of cardiac muscle reduction, completeness of LV release. The ESV increase reflects cardiac muscle insufficiency and promotes EDV augmentation in the subsequent cycles. The ESV increase, thus, is one of mechanisms of compensatory reaction realizations at a heart failure, in the form of involvement of Frank-Starling mechanism. Therefore at a stage of preoperative treatment for an adequate estimation of the operation forecast it is necessary to estimate dynamics of the systolic LV size. Reduction of the given indicator during preoperative preparation of patients with the complicated current aortal defect will testify sufficient safety of retractive function and reserve possibilities of a myocardium. The fraction of LV emission influenced the operation forecast in group of patients with AI ( $r=0,402$ ) more, than in a subgroup with AS ( $r=0,284$ ), whereas the indicator of fraction of shorting had almost identical influence on the forecast ( $r=0,406$  and  $r=0,387$  accordingly).



Almost all indicators of myocardial function parameters (F5) had average return correlation close to a strong one ( $r < -0,603$ ) (Fig. 4).

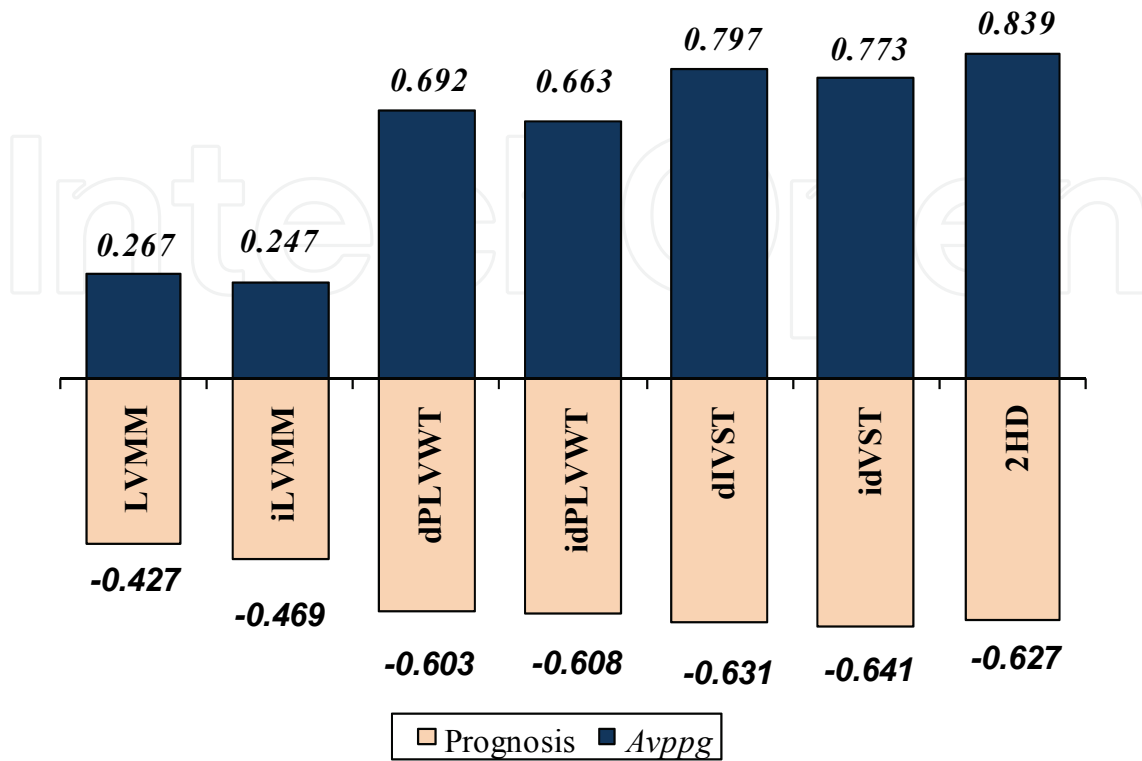


Fig. 4. Correlation of an indicator with the forecast and a systolic gradient of pressure

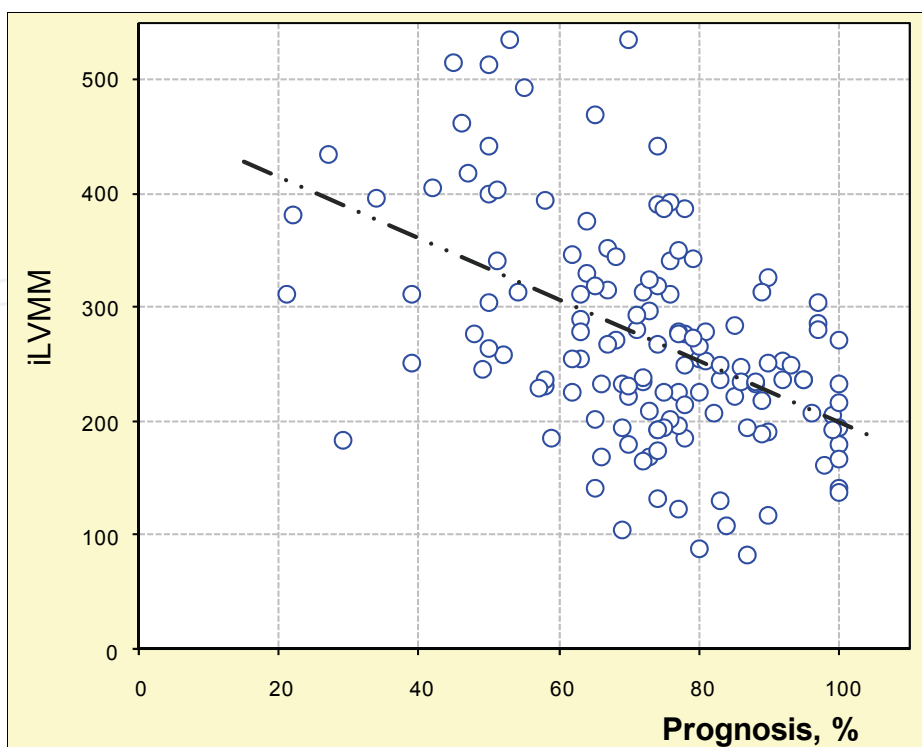


Fig. 5. Influence of an index of myocardium mass on the operation forecast

It has been revealed, that the expressed hypertrophy carries negative influence on the operation forecast. The lower the degree of a hypertrophy of LV walls, IVST and myocardium masses is, the better the operation forecast (Fig. 5). Great values of peak AVmpg ( $r > 0,663$ ) play a great role at expressed LV hypertrophy.

Correlation of indicators of myocardial function parameters (F5) on the forecast in hemodynamic groups has shown an identical direction of force of relation, with prevalence of size of correlation factor for group of patients with AS. In case of identical influence of value of LV myocardium mass on the operation forecast in hemodynamic groups ( $r = -0,407$ ), the degree of hypertrophy IVST ( $r = -0,459$ ) had more influence on the AS patients' operation forecast, than hypertrophy PLVWT ( $r = -0,281$ ) did. Whereas the forecast patients with AI have been influenced more by degree of hypertrophy PLVWT ( $r = -0,323$ ), than hypertrophies IVST ( $r = -0,131$ ). Evidence of IVST hypertrophy is bad prognostic sign, both at a stenosis of the aortal valve, and at its insufficiency. It is necessary to use surgical treatment of aortal defect at early stages of defect implication, before the expressed myocardium hypertrophy has development.

In spite of the fact that all patients had been executed with AV prosthetics, valve morphology variables (F6) (a calcification exponent ( $r = -0,563$ ), regurgitation degree on AV ( $r = 0,639$ ), changes on MV ( $r = -0,298$ ) and TV ( $r = -0,631$ )) had high degree of correlation. The expressed calcification and the related to it inflammatory process sometimes with transiting on ARD aortas and surrounding tissues, as a rule, found in patients with AS, leads to the loss of elastic properties and a destruction of elements of an aorta root, making the basic stages of operation more complicated to perform. At times after prosthesis implantation there is a high gradient on a prosthesis which reduces the possibilities of the return LV remodeling and retrogression of myocardium mass. In cases of AV insufficiency (patients with AI), enlarged ARD aortas and the sufficient sizes of LV cavity allow quickly in the conditions of good visibility to implant a larger prosthesis, even bigger than a settled one and to achieve the least transprosthetic gradient of pressure which promotes improvement of the current post-operative period.

Acknowledgement to it was the estimation of the influence of valve function parameters (F7) indicators which has shown, that the more the diameter of a root of an aorta is ( $r = 0,309$ ) and low indicators of initial AV mpg ( $r = -0,649$ ) are, the more accurate the operation forecast is. So the analysis of group of patients with AS has shown, that the operation forecast among patients with diameter of a fibrous ring more than 2,4 cm, which allowed to implant a prosthesis of adequate diameter without technical complexities, was more accurate. Whereas, in group with AI the operation forecast was more accurate among patients with no more than 3,5cm ARD diameter. Dilatation aorta ARD and expansion of an ascending aorta makes surgeons think about necessity of aortas binding or replacement of ascending department which leads to operation time extension and risk increase. The influence of a systolic gradient of pressure on the forecast has shown, that the higher its reference value is, the worse the operation forecast. If transprosthetic gradient of pressure does not exceed more than 30-40 mmHg in the postoperative period of prosthesis implantation, it allows achieving a favorable outcome of operation in more than 80 % of cases (Fig. 6).

#### 4. Discussion

Revealing of the indicators, which reference values can define the percent of a favorable outcome of operation, prognosticate possible complications, as well as an estimation of

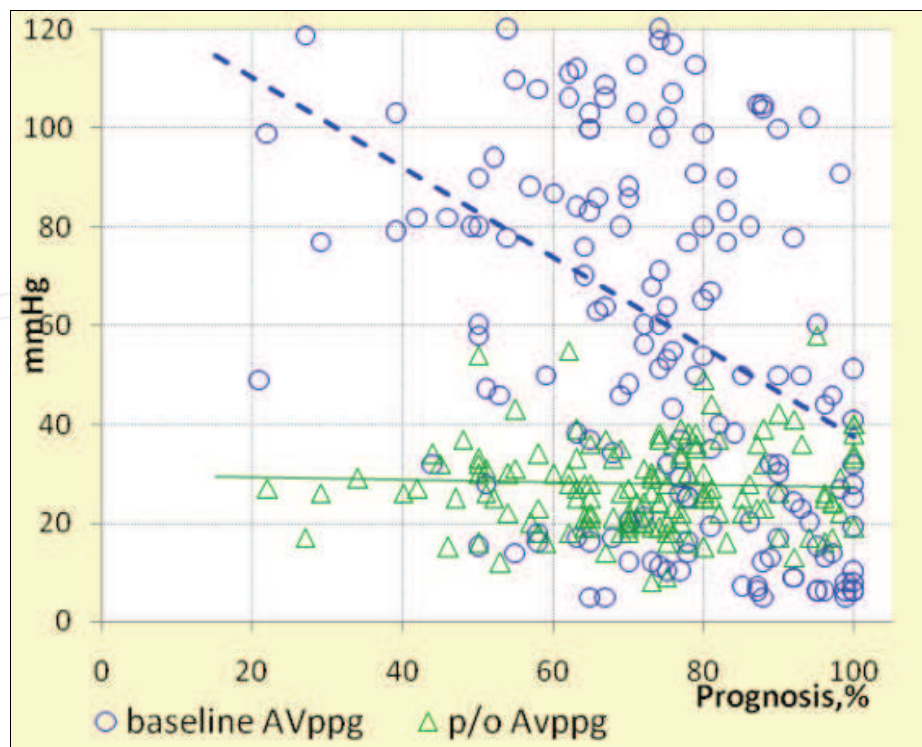


Fig. 6. Influence of a systolic gradient of pressure on the operation forecast

condition gravity in the preoperative period of patients to be operated is one of actual directions of modern cardio surgery. There are scales of risk estimation which sometimes limit an exact prediction of risk or which overrate the risk among patients who undergo valve surgery with or without coronary shunting [9,12,13,14,15]. There are intro-operative factors worsening the operation forecast: age, female gender, fraction of LV emission, HF, FC on NYHA, chronic obstructive diseases of lungs, a diabetes, chronic renal insufficiency [3,4]. There is convincing data, which say the risk of an early lethality increases if there is immediate surgery among patients of the senior age group and patients with an a trial clottage [5]. These indicators allow estimating results of a wide number of operations on heart. However the analysis and the account of indicators according to which it would be possible to estimate the forecast of operation of AV prosthetics in the postoperative period, taking into account initial data and specificity of operation are poor enough [10,11]. In our research 68 initial anatomic-functional indicators have been the subject of the correlation analysis. The carried analysis has allowed to group indicators in 7 basic groups of factors (F) and to define their influence on the operation forecast: the factor of disturbance of blood circulation (F1) - 4,9 %; the factor of anthropometrical indicators (F2) - 13,8 %; the factor of indicators of the central hemodynamic (F3)-24,2 %; the factor of anatomico-functional indicators of heart (F4)-26,5 %; the factor of indicators of myocardium LV (F5)-8,5 %; the factor of morphology of valves (F6)-6,9%, the factor of valves indicators (F7)-15,2 %. The correlation analysis has shown, that patients with less signs of heart failure ( $r = -0,346$ ), being in a smaller functional class, have more favorable the operation forecast. Thus these indicators for the operation forecast for patients with AI ( $r = 0,707$ ) was more important, than for group with AS ( $r = 0,580$ ). Patients of a smaller age group ( $r = -0,626$ ), with smaller Kettle index ( $r = -0,324$ ), having smaller value of a cardiothoracic index ( $r = -0,584$ ) had better operation forecast. Thus dependence on the forecast of operation from CTI was more among patients with AI ( $r = -0,567$ ). Whereas the influence of an indicator of body surface area on the

operation forecast was shown more among patients with AS ( $r=0,363$ ). Influence of indicators characterising a functional condition of the central hemodynamics had moderate correlation with the operation forecast ( $r=0,424$ ). One of significantly influencing the operation forecast is anatomic-functional indicators in both hemodynamic groups was SV ( $r=0,596$ ). The ejection fraction of LV influenced the operation forecast in group of patients with AI ( $r=0,402$ ) more, than in group with AS ( $r=0,284$ ). The most significant influence was exerted by the indicators characterizing the degree of a myocardium hypertrophies ( $r=0,839$ ), testifying that the operation forecast is mainly influenced by the condition of initial myocardium. IVST hypertrophy expression ( $r = -0,407$ ) is a bad prognostic sign, both in case of stenosis of the aortal valve, and at its insufficiency. Calcification expression AV ( $r = -0,563$ ), regurgitation degree on AV ( $r = 0,639$ ), changes in MV ( $r = -0,298$ ) and TV ( $r = -0,631$ ), expression of an initial systolic gradient of pressure ( $r = -0,649$ ) negatively affect the operation forecast. As a result of the carried out research there is the prognostic model with calculation of 14 various indicators, with prediction reliability of 75-90 % on the basis of which «the Program of forecasting of probability of a favorable outcome of surgical treatment of defects of the aortal valve» in medium "Excel - 2000" has been made and tested. This model is also devoted to forecasting of the surgical treatment results. Type of the realizing COMPUTER - personal computer Intel Celeron (2500 GHz), the programming language - "Visual Basic for Application", a kind and the version of operational system - Microsoft Excel - 2003 in a package «Microsoft Office 2003».

## 5. Conclusions

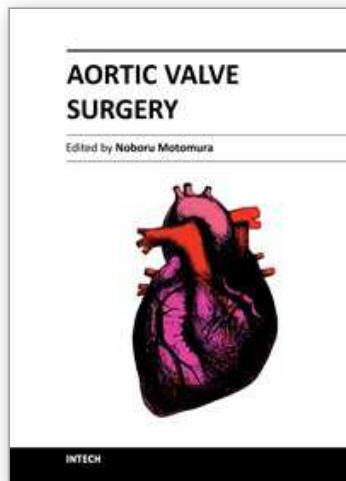
Thus, the carried out analysis of influence of initial anatomic-functional indicators on forecasting of results of the aortal valve prosthetics of has shown, that patients with an aortal stenosis and the prevalence of a stenosis are more serious group of defect with less favorable operation forecast, than patients with aortal insufficiency or prevalence of insufficiency. The reason of it is the expressed hypertrophy of LV and IVST having pathological character, with rasping morphological changes in AV in the form of calcification, with transition to FC aortas, the high indicators of a systolic gradient of pressure, with a forwardness of disturbances on a small circle of a blood circulation. Diameter of FC aortas of 2,3-3,5 sm is defined as the optimal size when AV prosthetics will give the best operation forecast as it will allow to implant the adequate prosthesis in both hemodynamic groups. With a smaller size of diameter of an aorta fibrous ring it is necessary to survey adequacy of the effective area of an implanted prosthesis. Value of a transprosthetic gradient of pressure less than 35-40 mm Hg after operation is considered to be optimum indicators which leads to positive results of prosthetics of the aortal valve.

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The aortic valve is located at the center of the heart. It is the core of cardiac anatomy and aortic valve surgery has led the field of cardiac surgery. This book describes all aspects of aortic valve surgery and it will help clarify daily questions regarding the clinical practice in aortic valve surgery, as well as induce inspiration and new insights into this field.

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